Reconsideration of the application is respectfully requested.

I. AMENDMENT

Please make the following amendments:

In the Claims:

Please cancel claim 8

Please amend the claims as follows:

C1 ~~10.~~ 8. (amended) The method of claim [9] 1, wherein the genomic region is located between markers D1S2681 and D1S2815.

~~11.~~ 9. (amended) The method of claim [9] 1, wherein the genomic region has a sequence contained in SEQ ID NO:1.

C2 ~~12.~~ 10. (twice amended) The method of claim 1, wherein the genomic region has a sequence contained in at least one genetic sequence selected from the group consisting of the [the] genetic sequences set forth in GenBank Accession # Z97876 (SEQ ID NO[.]: 7, SEQ ID NO[.]: 8 and SEQ ID NO[.]: 9), GenBank Accession # Z99943 (SEQ ID NO[.]: 10), and GenBank Accession # AL031733 (SEQ ID NO[.]: 7).

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-8, 10-15 and 17 were pending at the time of the present action. Of these, claim 8 has been canceled. Claims 10-12 have been amended. Therefore, claims 1-7, 10-15 and 17 are currently pending. The pending claims are reproduced in Appendix A for the Examiner's convenience.

B. The Action Improperly Fails to Accord the Application the Provisional Filing Date

The Action asserts that the Applicants have "not complied with one or more conditions for receiving the benefit of an earlier filing date." The Action contends that the application will be provided with the filing date of the present application because "the Examiner read the provisional application and did not find support for sequences recited in the claims and disclosed in the specification" and "the marker D1S2681 wherein the genomic region of the invention is comprised." Applicants respectfully traverse this allegation.

Applicants note that, as no prior art has been cited against the instant application, receiving the provisional filing date is not relevant to the prosecution of the application. Nevertheless, applicant's submit that while additional material was provided when the provisional application was converted to the instant application, it is nevertheless improper to assert that the full scope of the claims as currently pending were not taught by the original provisional application. Claim scope that is enabled by the initial provisional application should be accorded the earlier filing date under the requirements of 35 U.S.C. § 119(e). For example, claim 1 includes the limitation "said genomic region is comprised in chromosome 1q23.3-1q24" but does not limit the loci to D1S2681. The chromosomal region 1q23.3-1q24 as claimed is properly designated in the provisional application. Therefore, as the claim scope applies to this limitation, the earlier filing date is proper.

C. The Rejections under 35 U.S.C. § 101 are Overcome

The Action rejects claims 1-8, 10-15 and 17 under 35 U.S.C. §101 asserting that "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility based on screening for increased risk of developing hypercalciuria." Applicants respectfully traverse.

The Manual of Patent Examining Procedure sets forth the guidelines for compliance with the utility requirement of 35 U.S.C. § 101 in MPEP § 706.3(a)(1). Subsection (B)(1) makes it clear that an invention has utility if a particular purpose (*i.e.* "specific utility") is asserted by the specification and a person of ordinary skill would consider this assertion credible.

The specification at page 6, lines 11-15 states that: "[d]escribed in this invention is a method for screening for an increased risk of hypercalciuria by obtaining a sample nucleic acid from a subject; and analyzing the sample nucleic acid to detect the presence or absence of a genetic mutation in genomic region associated with an increased risk of developing hypercalciuria." The specific utility asserted by the application is thus the use of the claimed locus in screening for an increased risk of developing hypercalciuria. A person of ordinary skill would find this a credible assertion. The instant invention sets forth a genetic locus that is statistically related to an absorptive hypercalciuria phenotype in the screened kindred groups. The detection of the altered loci in an at risk individual would facilitate early detection of disease onset and potential intervention to allow for modifications in life-style or diet that could prevent or delay onset of the disease.

The instant specification sets forth the method for the localization of AH susceptibility to the 1q23.3-1q24 region of chromosome 1. The disclosure identifies a single locus on chromosome 1q23.3-q24 linked to an AH phenotype in three unrelated kindred which included individuals suffering from AH of varying severity. The inventors were able to establish a statistically significant linkage between an alteration in this loci and the AH phenotype. A person of ordinary skill would therefore reasonably recognize a correlation between the asserted utility and the ability to screen for AH as the instant specification sets forth a means of performing such screening and relates alternate methodologies that would also be applicable.

A person of ordinary skill would recognize that the instant invention provides substantive evidence that localizes a disease susceptibility phenotype to a specific genetic loci. Localization of a genetic loci is, in effect, a screening process. Therefore it would not require undue experimentation to perform similar screening on persons at risk for AH using methods similar to those set forth in the specification but restricted to the claimed loci. In its simplest embodiment, the instant invention may be carried out by performing screening procedures similar to those used for detecting the initial loci. In addition, a person of ordinary skill would be aware of more refined methods to screen for chromosomal deletions, alterations or other mutations.

Based upon the foregoing arguments, the rejection of claims 1-8, 10-15 and 17 under 35 U.S.C. §101 is in error. Applicants therefore respectfully request that this rejection be removed.

D. The Rejections under 35 U.S.C. § 112, First Paragraph, are Overcome

The Action rejects claims 1-8, 10-15 and 17 under 35 U.S.C. 112, first paragraph, asserting that "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility" and thus a person of ordinary skill would not know how to use the invention without undue experimentation.

Applicants have addressed the utility rejection above. Applicants however wish to reiterate that the specification sets forth a successful means of screening for an AH susceptibility loci. Applicants discovered a statistically significant linkage between a specific genetic loci and the AH phenotype in three familial groups. Genetic screening based upon the detection of disease susceptibility loci is a recognized and accepted methodology in the relevant art. One of ordinary skill would therefore recognize that a screening method for this altered loci would be

useful in detecting individuals potentially at risk for the development of AH or a related phenotype.

Further, it appears that the Action is attempting to couch an enablement rejection in terms of a §101 utility rejection. A rejection based on a lack of enablement must be adequately supported by substantive evidence. The PTO is required to assume that the specification complies with the enablement provisions of Section 112 unless it has "acceptable evidence or reasoning" to suggest otherwise. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-370 (CCPA. 1971). The PTO must therefore provide reasons supported by the record as a whole what the specification is not enabling. *Application of Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219-220 (CCPA 1979). Then and only then does the burden shift to the applicant to show that one of ordinary skill in the art could have practiced the claimed invention without undue experimentation. *In re Strahilevitz*, 668 F.2d. 1229, 1232, 212 USPQ 561, 563-64 (CCPA 1982). [Emphasis added]

The Action has erroneously placed the burden of proof on the Applicants without offering any evidence or reasoning based on the record as a whole why the disclosure is not enabling for the pending claims. The single "grounds" of rejection is without support and is couched in terms that a person of ordinary skill would not be enabled to carry out the invention because one of ordinary skill would have no way of recognizing a utility for the invention. As previously argued, the instant specification sets forth a means for screening for AH. Linkage analysis was performed in order to establish the correlation between the AH phenotype and the disclosed loci. A person of ordinary skill would understand that similar means to those taught by the specification could be employed to screen for the altered loci in other individuals deemed to be at risk for the development of the disease, *i.e.*, based on family history, as the specification

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teaches a successful means of screening (see examples 1 and 2). If the rejection is to be maintained under §112, the Examiner must support the noted position by citing published references or by Examiner's Affidavit, as required by MPEP 2144.03. In the absence of this support, this rejection cannot stand. Applicants therefore respectfully request that this rejection be removed.

E. The Rejections under 35 U.S.C. § 112, Second Paragraph, are Overcome

The Action rejects claims 1-12 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Applicants have amended claims 10-12 to more distinctly claim the invention. The amendments do not constitute new matter. Claim 8 has been canceled without prejudice or disclaimer.

Claim 10 and 11 have been amended to depend from a pending claim.

Claim 12 has been amended to incorporate the corrections cited by the Action.

Claim 1 is deemed indefinite by the Action because "species (a) does not define what mutation is being detected [and] [f]urthermore, it is unclear how species (b) relates to an increased risk." The Action further finds the claim indefinite because of the amendatory language previously submitted and because it is not demonstrated where the mutation causes increased risk.

Applicants submit that the standard being applied by the Action is improper. In order to satisfy the requirements of definiteness under §112, a claim, read in light of the specification, must reasonably apprise those of skill in the art of its scope. *See Amgen Inc. v. Chugai*

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Pharmaceutical Co. Ltd., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed.Cir.). The specification sets forth a standard means for successfully detecting the altered loci linked to the AH phenoytype, the specific mutated sequence is not necessarily relevant to the elucidation of an indicator of the AH phenotype. Linkage analysis successfully determined an altered loci linked to the AH phenotype. This, in and of itself, has utility in screening for AH susceptibility. While a "mutation" is obviously the basis of the detected chromosomal alteration, elucidation of the specific nucleotide change is not, at this point necessarily pertinent to the ability to successfully screen for the change. Nevertheless, the screening method that successfully detected the chromosomal change by linkage analysis is a "mutation" and thus the term is employed properly in the claim.

The Action apparently requires that the specification set forth the exact mutated sequence that leads to the development of the AH phenotype. This requirement is, however, not the threshold for patentability and is unnecessary to properly execute the invention within the scope of the claim. The specification sets forth a basic methodology for detecting the altered loci. One of ordinary skill would further recognize that a variety of commonly practiced screening procedures could be carried out to detect AH susceptibility based upon the recognition of the significance of the disclosed loci. Furthermore, based upon the derivation of the role of the disclosed loci, it would not require undue experimentation nor any inventive input to detect specific mutated sequences within the disclosed loci that might further relate to the development of the AH phenotype.

It is unclear what the Action deems objectionable about the amendatory language or why the failure to "demonstrate[] where the mutation causes increased risk" is an issue in the determination of definiteness. Applicants request that the Examiner specifically point out how

these elements are a basis for maintaining the instant rejection, or alternatively, consider them moot in light of the above arguments.

Based upon the foregoing arguments, the rejection of claims 1, and 10-12 under 35 U.S.C. §112, second paragraph is in error. Applicants therefore respectfully request that this rejection be removed.

III. PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136(a), Applicant petitions for an extension of time of one month to and including August 12, 2000 in which to respond to the Office Action dated April 14, 2000. Pursuant to 37 C.F.R. § 1.17, a check in the amount of $55.00 is enclosed, which is the process fee for a one-month extension of time. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Assistant Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski Deposit Account No. 50-1212/10017634/HAS.